STRUCTURE DETERMINATION OF ORNITHINE-LINKED CISPLATIN BY INFRARED MULTIPLE PHOTON DISSOCIATION ACTION SPECTROSCOPY

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Cisplatin $[(NH_3)_2PtCl_2]$, the first FDA-approved platinum-based anticancer drug, has been widely used in cancer chemotherapy. Its pharmacological mechanism has been identified as its ability to coordinate to genomic DNA with guanine as its major target. Amino acid-linked cisplatin derivatives are being investigated as alternatives for cisplatin that may exhibit altered binding selectivity such as that found for ornithine-linked cisplatin (Ornplatin, $[(Orn)PtCl_2]$), which exhibits a preference for adenine over guanine in RNA. Infrared multiple photon dissociation (IRMPD) action spectroscopy experiments and complementary electronic structure calculations are performed on a series of Ornplatin complexes to elucidate the nature of binding of the Orn amino acid to the Pt center and how that binding is influenced by the local environment. The complexes examined in the work include: $[(Orn-H)PtCl_2]^-$, [(Orn)PtCl]$^+$, $[(Orn)Pt(H_2O)Cl]^+$, and $[(Orn)PtCl_2+Na]^+$. In contrast to that found previously for the glycine-linked cisplatin complex (Glyplatin), which binds via the backbone amino and carboxylate groups, binding of Orn in these complexes is found to involve both the backbone and sidechain amino groups. Extensive broadening of the IRMPD spectrum for the $[(Orn)Pt(H_2O)Cl]^+$ complex suggests that either multiple structures are contributing to the measured spectrum or strong intra-molecular hydrogen-binding interactions are present. The results for Ornplatin lead to an interesting discussion about the differences in selectivity and reactivity versus cisplatin.